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Original Communication

Chronic drug use confirmed by hair analysis: Its role in understanding both the medical cause of death and the circumstances surrounding the death

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ABSTRACT

Analysis of hair for drugs is now a well established technique. It is being used increasingly in crime investigation but seldom in routine Coroner's toxicology. Hair analysis is the only method of obtaining a reliable drug history for the weeks or months prior to death.

Between 2004 and 2006 from the cases reported to HM Coroner, hair was submitted for analysis in addition to the routine specimens for 286 selected cases. These were all cases where drug use was thought to be involved in the death. The usefulness of the data from hair analysis was evaluated along with the data from the conventional samples. The types of cases were identified where hair analysis provided valuable supporting evidence.

It was found that reliable information concerning long-term drug use was important in a wide range of cases including: – demonstrating a history of drug use or lack of it, demonstrating tolerance or lack of it, compliance with medication, death due to long-term cocaine use and its role in depression/suicide, sudden unexplained death, and excited delirium. The cases types are illustrated by reference to individual cases and the implications of the findings discussed.

The study demonstrated that hair analysis can provide vital evidence in a wide range of cases reported to HM Coroner. This evidence can be invaluable to the pathologist, Coroner, and the family of the deceased in understanding both the medical cause of death and the circumstances surrounding the death.

1. Introduction

At a Coroner's post-mortem samples are taken for toxicological analysis from those cases where drug use/abuse may have influenced death. Traditionally these samples have included femoral vein blood, gastric contents, urine, and liver, and for certain cases, vitreous humor. However the analysis of these samples reveals only short term drug use, that is, the drugs used in the hours before death.

With the recent advances in technology it has become possible for analysis of hair for drugs to be used as a routine procedure. For example it is used routinely for verification of drug use history in child custody cases where a parent needs to show absence of drug use. In Germany and Italy if a person has their driving licence refused, withdrawn or suspended because of drug related offences, before the licence is returned drug abstinence must be proved and hair analysis is mandatory for this purpose.[1] Hair reveals a person's long-term drug history. Drugs are incorporated into hair at the growing point; they pass from the blood circulating the follicle into the hair shaft at the root tip. Once the drug is incorporated into the hair it is fixed, and it stays fixed in the hair as it grows. This produces a "tape-recording" of drug use over time. Hair grows at a rate of between 0.32 and 0.46 mm/day with a mean rate of growth of 1 cm per month used by analysts for interpretive purposes.[2] Head hair is the recommended sample for analysis, but if it is not available then hair from other body sites can be used. However, hair from other sites on the body will have different growth rates making it more difficult to interpret the time period of drug ingestion.[3]

There have been several papers suggesting the value of hair analysis in post-mortem toxicology including papers by Kintz,[4] Kronstrand et al.,[5] and Couper et al.,[6] but to date there has been no study using hair analysis as an adjunct to Coroner's post-mortem toxicology.

The Toxicology Unit at Imperial College London developed a method for the simultaneous detection and quantification of the major drugs of abuse and their metabolites.[7] These include amfetamine, metamfetamine, methylenedioxymethamfetamine (MDMA or ecstasy), methylenedioxyamfetamine, morphine, 6-monoacetylmorphine, codeine, dihydrocodeine, cocaine and its mteabolites benzoylecgonine and ecgoninemethylester, cocaethylene (formed

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when ethanol and cocaine are ingested simultaneously), diazepam and its metabolite desmethyldiazepam. These compounds are analysed from a single extraction and a single injection onto the gas chromatograph–mass spectrometer (GC–MS) using selective ion monitoring mode (SIM). A full screen for other drugs can then be carried out on the same extract by injecting a further aliquot using the GC–MS in scan mode. The complete analysis can be carried out using a single 20–50 mg sample of hair making the method ideally suitable for Coroner's work. The method which was fully validated and previously described elsewhere[7] was used to analyse all samples in this study.

Since 2004, in addition to the more traditional samples, hair has regularly been submitted from selected cases covered by the Coroner's jurisdiction of Eastern District of Greater London. The usefulness of the data from hair analysis was evaluated along with data from the conventional samples for the 286 cases submitted between 2004 and 2006. Presented here are the types of cases, illustrated by reference to individual cases, where analysis of hair has assisted the pathologist in establishing the cause of death, and the Coroner in reaching a verdict. The results of hair analysis were considered in combination with all other relevant information. The implications of the findings are discussed.

1.1. Collection of hair samples

A protocol for collection of post-mortem hair samples was issued to all the mortuary staff and pathologists concerned with collection of the hair samples. The protocol stated that the hair was to be collected before the start of the examination to avoid contamination with blood; the sample was taken from the posterior vertex of the head as this is the area where hair growth is least variable. The hair was to be cut as close to the scalp as possible and the cut ends kept aligned and wrapped in the foil which was provided. The foil was to be placed in a tamper proof bag for transportation to the laboratory. The protocol advised that the hair was not to be plucked and was not to be sent with the scalp attached. It also stated that if head hair was not available then pubic, axial or chest hair could be collected. If any of the above procedure had not been followed this was noted in the case file and an appropriate comment was included in the final report.

1.2. Summary of analytical procedure

The hair was segmented, shampoo washed and solvent washed. After drying it was cut into 1 mm lengths and the drugs were extracted by incubating overnight with dilute acid. This was followed by a clean-up stage using solid-phase extraction with mixed-mode cartridges. After derivatisation with MSTFA and MBTFA the extracts were analysed using GC–MS.[7] The washes were always analysed to check for environmental contamination.

2. Case types where analysis of hair for drugs has provided valuable supportive evidence

2.1. Demonstrating a history of drug use

In 76 of the 286 cases the hair sample was from a death involving heroin use. This was determined by standard toxicological analysis of post-mortem blood and urine. Sometimes with these cases the family denies that the deceased was a drug user, and they may also claim that it must have been the first time of use and suggest that someone could have assisted the deceased. If such allegations are made they require investigation by the police. As drug users can be very adept at concealing their habit such investigations may not confirm a previous history. However analysis of hair is a reliable way of determining a person's previous drug use or exposure to drugs and is more cost effective and less time consuming than a police investigation. In addition evidence showing an accurate drug history can often help the family come to terms with the death.

A case illustrating this involved a 24 year old woman found by her boyfriend dead in bed. Analysis of blood taken at post-mortem showed ingestion of a potentially fatal amount of methadone and alcohol. The family and her boyfriend strongly denied any previous drug use at all by the deceased. Analysis of hair demonstrated use of cocaine and ecstasy during the 6 months prior to death but no previous use of methadone. Faced with this evidence her boyfriend conceded that the deceased did have a history of cocaine and ecstasy use but not methadone.

2.2. Demonstrating abstinence from drug use

Family or friends often allege long-term abstinence from drugs by the deceased. Abstinence can readily be verified by hair analysis.

For example, a 29 year old male was found dead in the bathroom and a used syringe was found underneath the body. The deceased was a former addict, but the family believed he had not used heroin in the previous 3 years. Analysis of post-mortem blood demonstrated ingestion of a potentially fatal dose of heroin in combination with ethanol, dihydrocodeine, and cocaine. Analysis of pubic hair, which was on average 5 cm long, giving a drug history for approximately the 7 months prior to death showed ingestion of dihydrocodeine and cocaine but no heroin. Although analysis of hair did not assist in establishing the cause of death, it did confirm the family's belief that the deceased had not been using heroin at least not in the 7 months prior to death.

2.3. Demonstrating lack of tolerance

Tagliro et al. first suggested using hair morphine concentrations to verify a possible correlation between fatal heroin overdoses and the addiction behaviour of the individual before death.[8] Whether a concentration of morphine found in post-mortem blood is consistent with ingestion of a fatal dose of heroin or morphine depends on the tolerance of the individual. There is no way of measuring tolerance but evidence of repeated drug use can show the development of tolerance. For a heroin user quantifying the amount of morphine and 6-monoacetylmorphine present in hair can show whether the deceased was a light, moderate or heavy user of the drug and this can help with interpretation of results from the analysis of blood.

A case which illustrates this point concerns an 18 year old male found dead in bed. He had a history of alcohol use and drug abuse. The post-mortem blood morphine concentration was 0.32 μg/mL. This is within the normal range found in a regular user of heroin but is consistent with ingestion of a fatal amount in a naïve user. Analysis of head hair which was 1 cm in total was negative for 6-monoacetyl morphine and had morphine present at a concentration of less than 5 ng total. This showed that the deceased was a non-habitual user of heroin or had only occasionally taken a morphine-containing preparation and so had little tolerance. Analysis of hair provided evidence to support the interpretation that death was due to morphine toxicity. The hair was negative for other opioids including codeine, dihydrocodeine, tramadol, propoxyphene, and methadone demonstrating lack of cross tolerance.

2.4. Compliance with medication

Table 1 shows the drugs that have so far been detected in hair using the GC–MS in scan mode and includes anticonvulsants, antidepressants, and antipsychotics. This suggests the possibility of being able to find out whether or not the deceased had been taking their prescribed medication. Analysis of hair cannot show detail

Table 1
Drugs detected in hair using the GC–MS scan mode

Analgesics	Paracetamol, dextropropoxyphene + metabolite, tramadol
Anticonvulsants	Carbamazepine, phenytoin,
Antidepressants	Amitriptyline + metabolite, citalopram + metabolite, dosulepin + metabolite, fluoxetine, mirtazapine, paroxetine, sertraline, venlafaxine + metabolite
Antiemetics	Cyclizine
Antihistamine	Diphenhydramine
Antipsychotics	Olanzapine, quetiapine, thioridazine
Local anaesthetic	Lidocaine
Miscellaneous	Caffeine, nicotine
Other DOA	Methadone + metabolite, papaverine (can be used to show use of street heroin)
Used for HIV	Nevirapine

such as exactly what dose and whether the medication had been taken at the prescribed times, but it can show in general terms whether any drug had been taken and a negative finding would suggest that they had not been taking any medication on a regular basis.

One interesting case where compliance was an issue, concerned a 22 year old woman who was seen to walk on to the train track, the train struck her and she died from multiple injuries. The deceased was being treated for depression and was prescribed citalopram. The results for the segmental analysis of her hair shown in Table 2 indicate that the deceased had been taking her antidepressant medication throughout the 12 month period prior to death, but she had also been taking cocaine throughout this time and a small amount of a morphine-containing preparation in the 6 months prior to death. The results suggest that although the deceased had been taking her prescribed medication, her depression might have been exacerbated by her continued use of cocaine.

Table 2
Analysis of head hair demonstrating compliance with prescribed medication

Drug	Concentration ng/mg hair			
	Section 1	Section 2	Section 3	Section 4
MDMA (ecstasy)	0.1	<5ng total[a]	<5ng total[a]	Negative
Cocaine	5.9	8.1	10.3	10.6
Benzoylecgonine (BE)	0.5	0.6	0.6	0.7
Ecgoninemethylester (EME)	0.8	0.3	0.2	0.4
Morphine	<5 ng total[a]	<5 ng total[a]	Negative	Negative
Citalopram	Positive	Positive	Positive	Positive
Citalopram metabolite	Positive	Positive	Positive	Positive

Each section was 3 cm long; section 1 was closest to the scalp.
BE and EME are cocaine metabolites.
[a] Limit of quantification = 5 ng total, limit of detection = peak height 3× greater than baseline noise.

2.5. Depression/suicide related to chronic cocaine use

Use of cocaine is widespread and increasing. Tolerance and dependence to cocaine can happen very rapidly. As tolerance increases, the effects of the "highs" become shorter and less intense, even with increasing doses. This causes the user to "binge", that is, to take a large amount of the drug over a relatively short period of time. Following this bingeing withdrawal symptoms occur which are characterised by intense unpleasant feelings of lassitude and depression. This depression can be associated with suicidal intention. Following chronic use of the drug adverse psychological effects commonly follow, including anxiety and a depression with panic and hopelessness which may lead to suicidal thinking and behaviour in many cocaine users.[9]

Out of the 286 cases analysed in this study 36 of the deaths occurred as a result of self-suspension (hanging). Analysis of hair showed regular use of cocaine in 15 of these 36 cases. The analysis of the hair gave rise to the consideration of whether the depression leading to the suicide could have been a consequence of depression associated with chronic cocaine use. The results of the analysis of hair, post-mortem blood, and urine are shown in Table 3. For one case hair only was available. In 7 of the remaining 14 cases there was no cocaine or metabolite in either the post-mortem blood or urine. In these cases there may have been no mention of cocaine use in the history and therefore no reason to consider that the suicide might be linked to chronic cocaine use had the hair not been analysed and cocaine found.

2.6. Excited delirium

The term "excited delirium" was first used in 1849 to describe psychiatric patients who developed continuous agitation and mania in the presence of fever then collapsed and died.[10] The first modern mention of cocaine-associated excited delirium was in 1985.[11] Excited delirium is characterised by the acute onset of bizarre or violent behaviour including aggression, combativeness, hyperactivity, extreme paranoia, hallucinations, superhuman strength, or incoherent shouting. Hyperthermia is frequently pres-

Table 3
Analytical results for cases of self-suspension where cocaine was detected in hair

Case	Drugs in hair	Time window of hair growth	Drugs in blood	Drugs in urine
1	Cocaine + metabs	6 weeks	Alc, cocaine + metabs	Cocaine + metabs
2	Cocaine + metabs	2 months	N/A (decomposed body)	N/A
3	Cocaine + metabs	3 months	Alc, cocaine + metabs + MDMA	Alc, cocaine + metabs + MDMA
4	Cocaine + metabs	6 months	Alc, negative for drugs	N/A
5	Cocaine	7 months	Alc, negative for drugs	Alc, negative for drugs
6	Cocaine + metabs	8 months	Negative	Cocaine metabs
7	Cocaine + metabs	9 months	Citalopram only	N/A
8	Cocaine + metabs	2 years	Alc, negative for drugs	N/A
9	Cocaine + metabs/MDMA	3 months	Alc, cocaine + metabs	Alc, cocaine + metabs
10	Cocaine + metabs/MDMA	4 months	Alc, negative for drugs	Cocaine metabs, morphine
11	Cocaine + metabs/MDMA	5 months	Negative	N/A
12	Cocaine + metabs/MDMA	7 months	Alc, Cocaine + metabs	Alc, cocaine metabs
13	Cocaine + metabs/MDMA	8 months	Alc, cocaine + metabs + MDMA	Alc, cocaine + metabs + MDMA
14	Cocaine + metabs/MDMA (+heroin, benzodiazepines, citalopram)	9 months	Alc, negative for drugs	N/A
15	Cocaine + metabs/amphet	4 months	Alc, negative for drugs	N/A

Pubic hair was analysed for cases 6, 9, 12, 13. All others were head hair Alc = alcohol, amphet = amfetamines, metabs = metabolites, N/A = not available, MDMA = methylenedioxymethamfetamine or ecstasy.

ent. In Miami cocaine-associated excited delirium is responsible for approximately 10% of all cocaine deaths.[12] As one of the manifestations of the syndrome is displaying violent or aggressive behaviour, in many cases the police are called and a number of the deaths occur while the person is being restrained or in police custody. Death occurring in such circumstance can have far reaching repercussions both for the police officers involved and in public confidence in the police.

Cocaine-associated excited delirium is not associated with high concentrations of cocaine in the blood. A study carried out by Karch et al. in 1998 showed that cocaine blood concentrations in 51 trauma victims, where the presence of cocaine was an incidental finding, were not much lower than in the victims of excited delirium.[13] A study by Ruttenber et al. in 1999 concluded that the syndrome is caused by changes in dopamine processing induced by chronic and intense use of cocaine rather than by the acute toxic effects of the drug.[14] Analysis of blood and urine demonstrates acute drug ingestion; hair analysis is needed to demonstrate chronic drug use.

Three cases of death caused by cocaine-associated excited delirium were identified in this study.

2.6.1. Case one

A 27 year old male had been with his brother drinking and taking cocaine. After arguing with his brother the deceased went on the rampage in the street, head butting lamp posts and cars. A security guard was called and the deceased was restrained by keeping him face down on the floor with his hands behind his back. By the time the police arrived the deceased had ceased breathing.

2.6.2. Case two

Police were called to the high street where it had been reported that a 32 year old male was rolling in the road rambling incoherently and clutching at passing cars. He was conveyed to hospital. ECG revealed ischemic changes to the heart shortly before he died.

2.6.3. Case three

A 29 year old male was found dead in his bedroom. The bedroom had been totally ransacked although there were no other disturbances to the house.

In all three cases a complete toxicological analysis of either antemortem blood taken just before death or blood taken at post-mortem was carried out. The concentration of cocaine in each of the cases was not sufficiently high to have caused death due to acute cocaine toxicity, that is, it was not in the range found for example in drug mules where a package bursts.

Cocaine was detected in the hair from each of the deceased confirming chronic use of the drug. The metabolites of cocaine were detected demonstrating that the drug had been ingested and that the cocaine present was not due to surface contamination. The analysis of hair provided evidence to support the cause of death as cocaine-associated excited delirium. This evidence is of particular significance in cases where the deceased dies whilst being restrained or in police custody.

2.7. Sudden unexplained death – heart abnormalities arising from chronic cocaine use

Cocaine causes vascular disease and in general there is little to distinguish cocaine-induced vascular disease from naturally occurring vascular disease. Myocardial infarction is a relatively frequent complication of cocaine use. Chronic cocaine use also causes changes in the smaller coronary vessels highly reminiscent of changes seen in hypertensive individuals.[15] Therefore it is vital to get a reliable drug history in order to distinguish heart disease caused by chronic cocaine use from naturally occurring heart disease.

2.7.1. Case one

A 40 year old male was found dead at home. He had a past history of using cannabis and cocaine. The findings at post-mortem showed hypertrophic heart disease and coronary artery atheroma, but in view of the history of drug use blood and urine were taken at post-mortem; cocaine and its metabolites were detected in the urine only. Analysis of a 3.5 cm length of head hair showed continued use of cocaine throughout the 3.5 months prior to death.

2.7.2. Case two

A 36 year old male, a known IV drug user on a methadone programme, was taken to hospital because of pains in his legs. He collapsed, there was a massive pulmonary embolism, he was thrombolised but had a cardiac event. Analysis of blood and urine taken at post-mortem revealed possible toxic concentrations of morphine (from heroin) and methadone but no evidence of cocaine use. Analysis of a 4 cm length of head hair showed very high concentrations of cocaine and confirmed heroin use in the 4 months prior to death.

2.7.3. Case three

A 40 year old male was found dead at his home address. The major findings at post-mortem included coronary artery disease and a dilated flabby heart. The cause of death was given as acute myocardial infarction with coronary atherosclerosis but the family believed drugs were involved. Analysis of blood taken at post-mortem contained cocaine at a concentration consistent with recreational use and no other drugs were detected. Analysis of a 2 cm length of head hair showed cocaine use in the 2 months prior to death.

2.7.4. Case four

A 39 year old male was involved in a violent domestic incident during which it was alleged that he feigned a heart attack. He was conveyed to hospital but died shortly after admission. Findings at post-mortem included a large heart, ischemic changes, and coronary artery atheroma. The cause of death was provisionally given as ischemic heart disease with coronary artery disease. The deceased did have a past medical history of high cholesterol and had a strong family history of heart problems. However as part of the police investigation into the alleged assault the hair was analysed. Analysis of a 6 cm length of head hair showed use of cocaine in the 6 months prior to death.

Only one of the four cases had known genetic predisposition to heart disease. Analysis of hair confirmed regular cocaine use in all four cases and it must be concluded that chronic cocaine use could have caused, or at least exacerbated heart disease in these cases. This has significant implications for the families of the deceased who might otherwise be extensively and unnecessarily investigated for hyperlipidaemia etc.

2.8. Problems associated with hair analysis

There are problems associated with hair analysis but in practice these do not prevent its use as a technique for determining long-term drug history.

The major factor for consideration when interpreting the results of hair analysis is environmental contamination. Drug on the surface of the hair can be absorbed into the hair shaft. For this reason hair is solvent washed prior to extraction and these washes are analysed. If any drugs are found in the washes then the possibility of environmental contamination should be considered.[16]

Drugs are not only absorbed into hair from the blood at the root tip, they can also be absorbed into hair from sweat, or from sebum coating the hair. This can be from the individual or exchanged from person to person through intimate body contact. The concentrations found in sweat or sebum are so low[17–19] that the amounts

of contamination that could be transferred by person to person contact would not be sufficient to be detected by the method used for the analysis of hair in this study.

Drugs can be absorbed by passive inhalation, for example, when present in a room where crack cocaine is being smoked. This will result in cocaine being absorbed because of surface contamination and being ingested by inhalation. The amount of drug ingested by passive inhalation is so low it would not lead to concentrations in hair which would be detected by the method used for this study.

In order to show that the drug has entered the body, metabolites as well as parent drug have to be detected in hair for most drugs.[20]

Cosmetic treatment of the hair should always be considered.[21] Shampooing causes only a slight decrease in drug concentration in the hair matrix, but perming, bleaching, and dyeing hair can cause a partial loss of drug substances from the hair. This is because these treatments cause changes in the molecular structure of the hair pigment as well as damage to the cuticle. These treatments do not remove the drug from hair completely, but they can reduce the amount present so that it becomes too low to be detected. Also as these treatments cause damage to the cuticle the hair would become more susceptible to drug absorption from surface contamination.

As drug incorporation into hair is associated with melanin, it is thought that dark haired individuals have higher drug content in hair than fair haired individuals when using a drug at the same rate. This has been shown to occur with codeine use.[22] However recent studies by Uhl and Scheufler concluded that there is no substantial hair colour bias.[23]

3. Conclusion

Evidence concerning long-term drug use can be as important in helping to establish the cause of death and reaching a verdict as evidence concerning acute drug ingestion. Blood, urine, and other specimens which give evidence concerning the drugs taken within hours of death are routinely analysed in Coroner's work, but analysis of hair, which may provide evidence of drug use in the weeks or months prior to death, is not a routine procedure. The results of this study suggest that analysis of hair as an additional routine procedure in Coroner's work should be considered for particular case types.

Cocaine use is widespread, but deaths associated with its use may go undetected. Cocaine causes very few acute deaths, but chronic use may cause fatal cardiac disease and may be linked to depression leading to suicide. Providing supporting evidence of chronic drug use can be useful in these types of cases.

Analysis of hair provides a reliable drug history for the weeks or months before death which is helpful for the pathologist, Coroner, and the family of the deceased in understanding both the medical cause of death and the circumstances surrounding the death.

Conflict of interest statement

None of the authors have any conflicts of interest with respect to this study.

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Ethics

The study was approved by Riverside Research Ethics Committee.

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